Docket No.19240,431-US1

Applicants: Wei Gu et al. Application No.: 10/813,177

Filed: March 29, 2004

Amendments to the Claims

1-46. (canceled)

47. (presently amended) A method for determining whether an agent modulates a Mdm2-herpesvirus-associated ubiquitin-specific protease (HAUSP) interaction, comprising the steps of:

- (a) obtaining or generating an in vitro system comprising Mdm2 and HAUSP;
- (b) contacting the in vitro system with a candidate agent; and
- (c) determining whether the candidate agent increases or decreases <u>a level of Mdm2-HAUSP protein complex interaction</u> in the *in vitro* system,

wherein determination of an increase or decrease <u>the level</u> of Mdm2-HAUSP <u>protein</u> <u>complex interaction</u> in (c) indicates that the agent modulates Mdm2-HAUSP interaction.

48. (presently amended) The method of claim 47, wherein the determining in step (c) comprises comparing the level of Mdm2-herpesvirus-associated ubiquitin-specific protease (HAUSP) protein complex interaction in the *in vitro* system of step (b) with a level of Mdm2-HAUSP protein complex interaction in a second *in vitro* system comprising Mdm2 and HAUSP in the absence of the candidate agent, wherein determination of an increase or decrease of the level of Mdm2-HAUSP protein complex interaction in the *in vitro* system of step (b) compared to the second *in vitro* system indicates that the agent modulates Mdm2-HAUSP interaction.

49 - 53. (canceled)

- 54. (presently amended) A method for determining whether an agent is reactive with Mdm2, comprising the steps of:
- (a) contacting a candidate agent with Mdm2, in the presence of herpesvirus-associated ubiquitin-specific protease (HAUSP); and

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(b) determining whether the candidate agent inhibits Mdm2-HAUSP <u>protein complex</u> formation interaction,

wherein determination of inhibition of Mdm2-HAUSP <u>protein complex formation</u> interaction in (b) compared to Mdm2-HAUSP <u>protein complex formation</u> in the absence of the agent indicates that the agent is reactive with Mdm2.

55 - 56. (canceled)

57. (presently amended) A method for determining whether an agent is reactive with herpesvirus-associated ubiquitin-specific protease (HAUSP), comprising the steps of:

- (a) contacting a candidate agent with HAUSP, in the presence of Mdm2; and
- (b) <u>determining</u> whether the candidate agent inhibits HAUSP-Mdm2 <u>protein complex</u> <u>formation</u> interaction,

wherein determination of inhibition of Mdm2-HAUSP <u>protein complex formation</u> interaction in (b) compared to Mdm2-HAUSP <u>protein complex formation</u> in the absence of the agent indicates that the agent is reactive with HAUSP.

58 - 60. (canceled)

61. (canceled)

- 62. (presently amended) A method for determining whether an agent modulates Mdm2-herpesvirus-associated ubiquitin-specific protease (HAUSP) interaction, comprising the steps of:
- (a) obtaining or generating a first <u>in vitro</u> system comprising Mdm2 and HAUSP, and a second *in vitro* system comprising Mdm2 and HAUSP;
 - (b) contacting the first in vitro system with a candidate agent;
- (c) contacting the second *in vitro* system with (i) the candidate agent and (ii) an antibody, or fragment thereof, that specifically binds Mdm2; and

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(c) determining a level of HAUSP activity in the first system and the second system,

wherein determination of an increase or decrease of HAUSP activity in the first *in vitro*

system compared to the second in vitro system indicates that the agent modulates Mdm2-

HAUSP interaction.

63. (presently amended) A method for determining whether an agent modulates Mdm2-

herpesvirus-associated ubiquitin-specific protease (HAUSP) interaction, comprising the steps

of:

(a) obtaining or generating a first in vitro system comprising Mdm2 and HAUSP, and

a second in vitro system comprising Mdm2 and HAUSP;

(b) contacting the first *in-vitro* system with a candidate agent;

(c) contacting the second *in vitro* system with (i) the candidate agent and (ii) an

antibody, or fragment thereof, that specifically binds HAUSP; and

(c) determining a level of Mdm2 activity in the first system and the second system,

wherein determination of an increase or decrease of Mdm2 activity in the first in vitro system

compared to the second *in vitro* system indicates that the agent modulates Mdm2-HAUSP

interaction.

64. (new) The method of claim 54 or 57, further comprising the steps of:

(c) contacting a cell with the candidate agent, wherein the cell comprises Mdm2,

herpesvirus-associated ubiquitin-specific protease (HAUSP), or p53; and

(d) determining whether the agent activates or increases, or inhibits or decreases, one

or more Mdm2-associated, HAUSP-associated, or p53-associated biological events in the

cell, compared to a cell not contacted with the candidate agent.

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